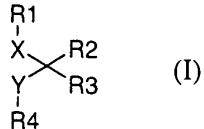


## CLAIMS

*a men.*  
*a 1*

1. A compound of general Formula I



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or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,  
wherein

$\text{R}_1$  represents,

$\text{C}_1\text{-C}_6$  alkyl, substituted with one or more basic groups such as amino, amidino and/or  
guanidino;

cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or  
guanidino;

heterocyclyl, containing at least one nitrogen atom;

heterocyclyl, containing at least one hetero atom selected from S or O,

and substituted with one or more basic groups such as amino, amidino and/or  
guanidino;

or aryl, substituted with one or more basic groups such as amino, amidino and/or  
guanidino,

$\text{R}_2$  represents H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl,

20 aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano,  
cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol,  $\text{Z}_2\text{N-}$   
 $\text{CO-O-}$ ,  $\text{ZO-CO-NZ-}$  or  $\text{Z}_2\text{N-CO-NZ-}$  group,

$\text{R}_3$  represents  $\text{COOR}_5$ ,  $\text{SO}(\text{OR}_5)$ ,  $\text{SO}_3\text{R}_5$ ,  $\text{P=O}(\text{OR}_5)_2$ ,  $\text{B}(\text{OR}_5)_2$ ,  $\text{P=OR}_5(\text{OR}_5)$ , or tetrazole,  
or any carboxylic acid isostere,

25  $\text{R}_4$  represents SH, S-CO-C<sub>1</sub>-C<sub>6</sub> alkyl or S-CO-aryl,

$\text{R}_5$  represents H, C<sub>1</sub>-C<sub>6</sub> alkyl or aryl,

$\text{R}_6$  represents H or C<sub>1</sub>-C<sub>6</sub> alkyl,

X represents O, S, SO, SO<sub>2</sub>, C(Z)<sub>2</sub>, N(Z), NR<sub>6</sub>SO<sub>2</sub>, SO<sub>2</sub>NR<sub>6</sub>, NR<sub>6</sub>CO or CONR<sub>6</sub>,

Y represents C(Z)<sub>2</sub>,

*contd.*

*a<sup>1</sup>*

~~X~~ represents independently H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, cycloalkyl or heterocyclyl.

2. The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

5 wherein

R<sub>1</sub> represents,

cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

10 heterocyclyl, containing at least one hetero atom selected from S or O, and substituted with one or more basic groups such as amino, amidino and/or guanidino; or aryl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

R<sub>2</sub> represents H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl,

15 aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol, Z<sub>2</sub>N-CO-O-, ZO-CO-NZ- or Z<sub>2</sub>N-CO-NZ- group,

R<sub>3</sub> represents COOR<sub>5</sub>,

R<sub>4</sub> represents SH, S-CO-C<sub>1</sub>-C<sub>6</sub> alkyl or S-CO-aryl,

20 R<sub>5</sub> represents H, C<sub>1</sub>-C<sub>6</sub> alkyl or aryl,

R<sub>6</sub> represents H or C<sub>1</sub>-C<sub>6</sub> alkyl,

X represents O, S, SO, SO<sub>2</sub>, C(Z)<sub>2</sub>, NZ, NR<sub>6</sub>SO<sub>2</sub>, SO<sub>2</sub>NR<sub>6</sub>, or CONR<sub>6</sub>,

Y represents C(Z)<sub>2</sub>,

Z represents independently H, C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, cycloalkyl or heterocyclyl.

25 3. The compound according to claim 1 or 2, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein

R<sub>1</sub> represents,

30 cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom

contd.  
a<sup>1</sup>

heterocyclyl, containing at least one hetero atom selected from S or O, and substituted with one or more basic groups such as amino, amidino and/or guanidino;

R<sub>2</sub> represents H, C<sub>1</sub>-C<sub>3</sub> alkyl, amino, halogen, hydroxy,

R<sub>3</sub> represents COOR<sub>5</sub>,

5 R<sub>4</sub> represents SH, S-CO-C<sub>1</sub>-C<sub>6</sub> alkyl or S-CO-aryl,

R<sub>5</sub> represents H, C<sub>1</sub>-C<sub>6</sub> alkyl or aryl,

X represents C(Z)<sub>2</sub>,

Y represents C(Z)<sub>2</sub>,

Z represents independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

10 4. The compound according to any previous claim, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein

15 R<sub>1</sub> represents,  
cycloalkyl, substituted with one or more basic groups such as amino, amidino and/or guanidino;

heterocyclyl, containing at least one nitrogen atom;

R<sub>2</sub> represents H, F, or C<sub>1</sub> alkyl,

R<sub>3</sub> represents COOR<sub>5</sub>,

20 R<sub>4</sub> represents SH, S-CO-C<sub>1</sub>-C<sub>6</sub> alkyl or S-CO-aryl,

R<sub>5</sub> represents H, C<sub>1</sub>-C<sub>6</sub> alkyl or aryl,

X represents C(Z)<sub>2</sub>,

Y represents C(Z)<sub>2</sub>,

Z represents independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

25 5. The compound according to any previous claim, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, wherein

R<sub>1</sub> represents cyclopentyl, pyridyl, pyrimidinyl, piperidinyl or thiazolyl,

R<sub>2</sub> represents H, F, or C<sub>1</sub> alkyl,

30 R<sub>3</sub> represents COOR<sub>5</sub>,

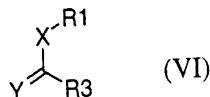
R<sub>4</sub> represents SH,

R<sub>5</sub> represents H,

contd.  
a<sup>1</sup>

~~X represents CHZ,  
Y represents CHZ,  
Z represents independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.~~

5 6. A process for the preparation of a compound according to any one of claims 1-5,  
wherein R<sub>1</sub>, R<sub>3</sub>, R<sub>4</sub>, and Y are as defined in claim 1 and X is C(Z)<sub>2</sub> and R<sub>2</sub> is H, comprising  
the step of;  
reacting a compound of Formula VI,

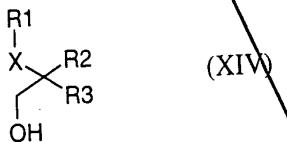


10 wherein R<sub>1</sub>, R<sub>3</sub> and Y are as defined in claim 1 and X is C(Z)<sub>2</sub>, with a compound of  
Formula IX,

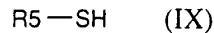


15 wherein  $R_5$  is a suitable protecting group, such as Ac, Bz, PMB or Bn, alone or in the presence of a suitable base, such as NaOMe, NaH or triethylamine or alternatively in the presence of a free-radical initiator, such as AIBN under standard conditions.

7. A process for the preparation of a compound according to any one of claims 1-5, wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> are as defined in claim 1 and Y is CH<sub>2</sub> and X is O, S, C(Z)<sub>2</sub>, or N(Z), comprising the step of:  
reacting a compound of Formula XIV,



wherein R<sub>1</sub>, R<sub>2</sub>, and R<sub>3</sub> are as defined in claim 1 and X is O, S, C(Z)<sub>2</sub>, or N(Z), with a compound of general Formula IX,



wherein R<sub>5</sub> is a suitable protecting group, such as Ac or Bz, in the presence of a suitable reagent, such as PPh<sub>3</sub>/DIAD, under standard conditions.

8. A process for the preparation of a compound according to any one of claims 1-5, wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, and Y are as defined in claim 1 and X is NR<sub>6</sub>CO, or NR<sub>6</sub>SO<sub>2</sub> comprising the step of:

10 reacting a compound of the general Formula XV,



wherein R<sub>2</sub>, R<sub>3</sub>, R<sub>6</sub> and Y are as defined in claim 1 and R<sub>5</sub> is a suitable protecting group, such as Ac, Bz, PMB or Bn, with a compound of the general Formula XVI,



15

wherein R<sub>1</sub> is as defined for in claim 1 and X is COOH or SO<sub>2</sub>Cl in the presence of suitable coupling reagents, such as PyBOP/DIPEA, DCC/HOBt, EDC/TEA/DMAP or pyridine, under standard conditions.

20 9. A pharmaceutical formulation containing a compound according to any one of claims 1 to 5 as active ingredient in combination with a pharmaceutically acceptable adjuvant, diluent or carrier.

10. The use of a compound according to any one of claims 1 to 5 in therapy.

*Amn. A2* 5  
11. The use of a compound according to ~~any one~~ of claims 1 to 5 for the manufacture of a medicament for the inhibition of carboxypeptidase U.

12. A method for treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising administering to a mammal, including man, in need of such treatment an effective amount of a compound as defined in any of claims 1-5.

10 13. A pharmaceutical formulation for use in the treatment or prophylaxis of conditions associated with inhibition of carboxypeptidase U, comprising a compound as defined in any of claims 1-5 in combination with a pharmaceutically acceptable adjuvant, diluent or carrier.

14. A pharmaceutical formulation, comprising:  
(i) a compound of Formula I or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, and  
15 (ii) one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P<sub>2</sub>T) antagonist,  
20 in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

15. A kit of parts comprising:  
(i) a pharmaceutical formulation containing a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and  
25 (ii) a pharmaceutical formulation containing one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P<sub>2</sub>T) antagonist,  
30 in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

*contd.**a 2*

which compound (i) and agent (ii) are each provided in a form that is suitable for administration in conjunction with the other.

16. A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a therapeutically effective total amount of

(i) a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; in conjunction with

(ii) one or more antithrombotic agent with a different mechanism of action, such as an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor or ADP-receptor (P<sub>2</sub>T) antagonist,

in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier.

17. A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a formulation as defined in claim 14.

*Add**a 3*